REMARKS

The pending Office Action addresses claims 1-7, 9, 10, 12-25, 27, and 28. Claims 1-6, 9, 10, 12, 13, 20, 23-25, 27, and 28 are rejected. Claims 7, 14-19, 21, and 22 are withdrawn from consideration. Reconsideration is respectfully requested in view of the following remarks.

Applicants acknowledge that when claims to the elected species are found allowable, claims withdrawn to a non-elected species that require all the limitations of the allowable claims will be considered for rejoinder. In the event of the rejoinder, the restriction requirement will be withdrawn and the rejoined claims will be fully examined for patentability in accordance with 37 CFR 1.104.

Amendments to the Claims

Applicants present the following amendments for the sole purpose of expediting prosecution of the pending claims. It is understood that such amendments are made without prejudice, and do not amount to Applicants' acceptance of the Office Action's rejections. Applicants reserve the right to prosecute any of the former forms of the claims in a continuing application.

Applicants amend claim 1 to recite that the at least one tissue fragment is combined with the isolated biological tissue slice. This amendment is made to clarify for the Examiner that the tissue slice and the at least one tissue fragment are separate components of the implant. Support for this amendment can be found throughout the published specification, for example at paragraphs 0040 and 0044.

Applicants amend claim 20 to recite applying the at least one minced tissue fragment to the isolated biological tissue slice to form a biocompatible implant. This amendment is also made to clarify for the Examiner that the at least one tissue fragment is a separate component that is applied to the tissue slice to form the claimed implant. Support for this amendment can be found throughout the published specification, for example at paragraph 0106.

No new matter is added.

Rejections Pursuant to 35 U.S.C. §102 and §103

The Examiner rejects claims 1-6, 9, 12-13, 20, 23-35 and 27-28 pursuant to 35 U.S.C. §102(b) as being anticipated by US Patent No. 6,485,723 to Badylak et al. ("Badylak") or, in the alternative, pursuant to 35 U.S.C. §103(a) as being unpatentable over Badylak. Applicants respectfully disagree with the Examiner's rejections.

Independent Claim 1

Claim 1 recites a biocompatible tissue implant for repairing a tissue injury or defect. The claimed three-part implant includes (a) an isolated biological tissue slice, (b) at least one minced tissue fragment, and (c) a retaining element. The at least one minced tissue fragment is combined with the isolated biological tissue slice. For example, minced tissue fragments can be added to an adhesive used to secure the implant or alternatively to a gel-like carrier applied to the implant. (See, e.g., paragraph 0040). The tissue slice is capable of acting as a cell source that allows viable cells to migrate out of the tissue slice. Similarly, the at least one minced tissue fragment also contains a plurality of viable cells that can migrate from the tissue fragment. Finally, a retaining element secures the tissue slice, and thereby the entire three-part implant, to the tissue site.

The Examiner continues to assert that Badylak "discloses a biocompatible tissue implant comprising a naturally occurring biocompatible tissue slice." The Examiner also asserts that "the tissue slice [includes] an effective amount of viable cells" and that "cells can migrate out of the tissue." However, claim 1 recites an isolated biological tissue slice, harvested from healthy tissue, that is capable of acting as a cell source. Badylak fails to teach or suggest a biological tissue slice harvested from healthy tissue that is capable of acting as a cell source. Badylak merely discloses a tissue graft construct that is formed from a submucosa matrix material. *See* Badylak at col. 2, lines 63-66 and col. 3, lines 59-61. First, the submucosal tissue that is processed into the submucosa matrix material is not harvested from healthy tissue, but is merely "a plentiful by-product of commercial meat production operations." *See* Badylak at col. 2, lines 25-29. Second, the submucosa matrix material disclosed by Badylak is not capable of acting as a cell source. The submucosa matrix material is produced by processing vertebrate intestinal material. *See* Badylak at col. 4, lines 1-14) Badylak discloses that the resulting submucosa matrix is substantially acellular after processing. *See* Badylak at col. 2, lines 30-33. Thus,

although Badylak teaches that the matrix can be seeded with cells prior to implantation, the source of the cells is not the acellular submucosa matrix. Badylak therefore fails to disclose an isolated biological tissue slice, harvested from healthy tissue, that is capable of acting as a cell source, as required by claim 1.

Furthermore, as amended, claim 1 also recites that the biocompatible tissue implant includes at least one minced tissue fragment containing viable cells that can migrate from the tissue fragment. At the outset, Badylak fails to teach or suggest an implant that includes at least one minced tissue fragment. Badylak merely discloses isolated and cultured cells that can be seeded onto the submucosa matrix. *See* Badylak at col. 3, lines 13-28. Isolated and cultured cells are very different from minced tissue fragments that contain viable cells. Thus, cells obtained through cell culture, even when seeded onto the submucosa matrix disclosed by Badylak, are not equivalent to the claimed tissue implant.

In the most recent Office Action, the Examiner now also asserts that:

> it would have been obvious to one having ordinary skill in the art at the time the invention was made to modify the plurality of layers of SIS by a layer of SIS that is made of a mince, tear, cut or any other cutting step similar to the ones describes above (as disclosed in another embodiment shown in col. 4, lines 43-50).

However, the modification suggested by the Examiner would not have been obvious to one of ordinary skill in the art. Badylak fails to teach or suggest adding or modifying the layered implant to include a layer of SIS that is minced, torn or cut. Badylak merely discloses a fluidized form of submucosal tissue that is prepared by "tearing, cutting, grinding, or shearing the harvested submucosal tissue." Badylak at Col. 4, lines 43-50. The final result is a "powder" that can be hydrated to form a submucosal fluid. *Id.* First, there is no teaching or suggestion that the submucosal fluid is added to a layered implant. Second, there is no teaching or suggestion that the torn, cut, ground, or sheared submucosal tissue is used except to make a submucosal fluid. In fact, the torn, cut, ground, or sheared tissue is merely an intermediate step in the production of the final submucosal fluid. Thus, one of ordinary skill in the art, relying on the teachings of Badylak, would not have modified the layered embodiment of Badylak to

include pieces of submucosal tissue from an intermediate step in the production of a submucosal fluid.

Furthermore, even if such a modification would have been obvious to one of ordinary skill in the art, it would fail to teach the claimed invention. Claim 1 requires that the at least one minced tissue fragment contains a plurality of viable cells that can migrate from the tissue fragment. The powdered submucosal tissue does not contain viable cells that can migrate from the powder because the powder is formed from harvested submucosal tissue that is substantially acellular. Thus, the powder itself does not contain viable cells. Even if cells are seeded onto the "solid or semi-solid matrix" formed from the fluidized submucosa, the powder granules themselves do not contain the cells. *See* Badylak at Col. 5, lines 47-54. To the contrary, the cells are merely cultured on the surface of the matrix formed from the fluidized powder. *Id*

The Examiner also erroneously interprets claim 1 to allow the minced tissue fragment to be part of the tissue slice or, alternatively, a section of the whole implant to be a minced tissue fragment. In particular, the Examiner states that:

> The Applicant's representative added at least one minced tissue fragment to the existing claims in order to overcome the previous rejection but the Applicant's representative used the word "associated" when relating the minced tissue fragment with the isolated biological tissue slice.
> The Examiner interpreted the word "associated as follow: ---to joint or to keep company with---. Therefore, the minced tissue fragment can be part of the tissue slice. **For example, the Examiner can interpret the whole implant (the whole SIS tissue) as the tissue slice, then the Examiner can interpret a section (a fragment) of the whole implant as the minced tissue fragment.** Therefore, the tissue fragment is associated with the tissue slice. (Emphasis added).

Such an interpretation is clearly contrary to the plain meaning of the claim, regardless of the particular term used to refer to the association between the tissue slice and the minced tissue fragment. Claim 1 recites a three-part implant comprising (a) an isolated biological tissue slice, (b) at least one minced tissue fragment, and (c) a retaining element. As amended, claim 1 also recites that the at least one minced tissue fragment is combined with the isolated biological

tissue slice. It is nonsense to assert that the one minced tissue fragment is just a part of the tissue slice itself. It is just as absurd to interpret a section of the whole implant as the minced tissue fragment. The claim clearly recites three separate elements, i.e., the slice, the fragment, and the retaining element. The claim also clearly recites that the fragment is combined with the slice and that the slice is secured to the tissue site by the retaining element. Thus, the claim clearly requires that the minced tissue fragment is a separate element from the tissue slice.

The Examiner then argues that Badylak discloses a layered implant and asserts that "one layer can be interpreted as the tissue slice and a second layer can be interpreted as the minced tissue fragment." This interpretation is also clearly erroneous. One of ordinary skill in the art would not interpret one layer of a layered implant according to Badylak to be a minced tissue fragment. The terms tissue slice and tissue fragment have entirely different meanings and refer to entirely different things. For example, Applicants disclose that the term slice "refers to a thin section, strip or sliver." Paragraph 0033. Applicants also disclose that tissue slices may be layered. *See* Paragraph 0043. However, the exemplary implant formed from layers of tissue slices can still be combined with minced tissue fragments. *See* Paragraph 0044. Thus, tissue slices and minced tissue fragments are entirely different from each other. Badylak only discloses an implant formed from layers of submucosal tissue, not a tissue slice combined with minced tissue fragments.

Regardless, even if Badylak's submucosa layers simultaneously form tissue slices and minced tissue fragments, which they clearly cannot, the Examiner's arguments regarding the submucosa layers fail to remedy the fundamental deficiencies of Badylak discussed above. In summary, Badylak fails to teach or suggest that any of the submucosa layers are harvested from healthy tissue or capable of acting as a cell source. As discussed above, Badylak discloses a submucosa matrix that is substantially acellular after processing. (*See* Badylak at col. 2, lines 30-33). Thus, the acellular submucosa matrix is not the source of the cells. Instead, the cells are seeded onto the implant prior to implantation.

Accordingly, independent claim 1 distinguishes over Badylak and represents allowable subject matter. Claims 2-6, 9, 12 and 28 distinguish over the cited art at least because they depend from claim 1.

Independent Claim 20

Claim 20 recites a method for repairing tissue injury or defect. The claimed method comprises providing (i) an isolated biological tissue slice harvested from healthy tissue that is capable of acting as a source of viable cells; and (ii) at least one minced tissue fragment containing a plurality of viable cells that can migrate from the tissue fragment. The method further comprises applying the at least one minced tissue fragment to the isolated biological tissue slice to form a biocompatible tissue implant. For example, minced tissue fragments can be added to an adhesive used to secure the implant or alternatively to a gel-like carrier applied to the implant. (See, e.g., paragraph 0040).

As discussed above, Badylak fails to teach or suggest a biological tissue slice harvested from healthy tissue that is capable of acting as a source of viable cells or at least one minced tissue fragment containing viable cells. Also as discussed above, Badylak fails to teach or suggest at least one minced tissue fragment containing viable cells that can migrate from the tissue fragment. Thus, claim 20 distinguishes over Badylak for at least the reasons discussed above with respect to claim 1. Furthermore, Badylak also fails to teach or suggest applying a minced tissue fragment containing a plurality of viable cells to the biological tissue slice as required by claim 20. The Examiner appears to argue that the torn, cut, ground, or sheared submucosal tissue disclosed by Badylak forms the claimed minced tissue fragment. However, as discussed above, there is no teaching or suggestion that the torn, cut, ground, or sheared submucosal tissue is used except to make a submucosal fluid. In fact, the torn, cut, ground, or sheared tissue is merely an intermediate step in the production of the final submucosal fluid. Furthermore, the fluidized embodiment is not used, in any form, with the layered embodiment. Instead, Badylak discloses that the fluidized submucosal tissue is gelled to form a solid or semi-solid matrix onto which cells can be seeded. *See* Badylak at Col. 5, lines 47-54. Thus, Badylak fails to teach or suggest applying the fluidized embodiment to any of the layered embodiments.

Accordingly, independent claim 20 distinguishes over Badylak and represents allowable subject matter. Claims 23-25 and 27 distinguish over the cited art at least because they depend from claim 20.

Dependent Claim 13

Claim 13 recites that the at least one minced tissue fragment has a particle size in the range of about 0.1 mm^3 to about 2 mm^3. At the outset, Applicants note that claim 13 incorporates the recitations of independent claim 1 and thus distinguishes over Badylak for at least the reasons discussed above with respect claim 1. The Examiner also admits that Badylak fails to disclose "particles sizes [sic] having a range of about 0.1 mm^3 to about 2 mm^3." The Examiner asserts that "[i]t would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the particle size since it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involve only routine skill in the art." At the outset, Badylak fails to disclose even the general conditions of claim 13. In particular, Badylak fails to teach or suggest an implant that includes even at least one tissue fragment containing a plurality of viable cells, much less a tissue fragment containing a plurality of viable cells that is of the claimed size range. Thus, Badylak lacks even the general conditions necessary for one of ordinary skill in the art to discover an optimum or workable range.

Furthermore, the Examiner has failed to make out a case of *prima facie* obviousness with respect to the use of routine optimization to obtain the fragment size range recited in claim 13. In particular, Badylak does not recognize the parameter of fragment size as a result effective variable. As the MPEP notes, only variables recognized as result effective can be optimized:

> A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. In re Antonie, 559 F.2d 618, 195 USPQ 6 (CCPA 1977).
>
> *See* MPEP § 2144.05 II. B.

As discussed above, Badylak fails to teach or suggest <u>any</u> range of fragment sizes, much less the claimed range of sizes. Thus, Badylak does not disclose or suggest that fragment size is result-effective nor does the Examiner indicate how the parameter of fragment size is result effective. There is, therefore, no recognition in Badylak that minced tissue fragment size has an effect on the success of an implant, or in other words, that fragment size would be result-

effective. Thus, Badylak fails to disclose to one of ordinary skill in the art either the general conditions of claim 13, much less that the parameters recited in claim 13 would have achieve a recognized result. Therefore the determination of an optimum or workable range of fragment sizes would not have been a matter of routine optimization to one of ordinary skill in the art.

Accordingly, claim 13 distinguishes over Badylak and represents allowable subject matter.

Conclusion

In conclusion, Applicants submit that all pending claims are now in condition for allowance, and allowance thereof is respectfully requested. The Examiner is encouraged to telephone the undersigned attorney for Applicants if such communication is deemed to expedite prosecution of this application.

The Director is hereby authorized to charge any deficiency in the fees filed, asserted to be filed or which should have been filed herewith (or with any paper hereafter filed in this application by this firm) to our Deposit Account No. 141449, under Order No. 22956-235.

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Respectfully submitted,

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